ISSN: 2634 - 680X

Journal of Clinical Case Studies, Reviews & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

COVID -19: Aetiology, Transmission, Receptor and the Third Wave Pandemic

Ali F C[1], Okolo RC[1,2,3], Ugwu I B [1,4] and Okoro B N[1]

[1]School of Medical Laboratory Technician, Bishop Shanahan Specialist Hospital Nsukka, Nigeria

[2]General Hospital Nsukka Enugu State Nigeria

[3]Department of Medical Laboratory Sciences, University of Nigeria Enugu Campus, Nigeria

[4]Department of Medical Laboratory sciences, Enugu State University of Science and Technology Teaching Hospital (Parklane), Enugu State, Nigeria

ABSTRACT

A wave of pandemic in an era of Covid-19 came in sinusoidal manner with a rise and fall in the outbreak resulting in rise in number of affected or infected people. The rise followed with limited knowledge and inadequate specialized equipment, preventive measures and the emergent of mutants led to multiple waves. The fall in the number of deaths led to state of relaxation, rise in economic and social activities led to second wave. The slight rise followed the failure to obtain general immunity and pharmacological intervention. And this led to the latest wave, the delta variant B.1.617 as the variant of concern (VOC) at stake. The virus is regarded as the seventh strain of corona virus family to induce infection in human. It uses the spike(s) protein found on their surface to recognize and bind specific receptors on host cell surfaces resulting in virus entry to the cell host and cause disease. This is a highly transmittable and pathogenic viral infection and attaches to the angiotensin converting enzyme 2(ACE-2) located in the vital organs and gives the virus access to have faster entrance to the system thereby getting the infected down easily. The review is to highlight what the covid-19 is all about and the uncertainties concerning the deceptive wave-like nature it took and to adopt the preventive measures to avoid another strange surge.

***Corresponding author**

Okolo Raphael Chinweike, School of Medical Laboratory Technician, Bishop Shanahan Specialist Hospital Nsukka, Nigeria. Tel: 08066795063. E-mail: okoloraph@gmail.com

Received: October 18, 2021; **Accepted:** October 25, 2021; **Published:** November 05, 2021

Keywords: Coronavirus, Angiotensin converting enzyme-2, Wave, Pandemic

List of Abbreviations

ACE2 – Angiotensin Converting Enzyme 2 ARDS – Acute Respiratory Distress Syndrome Cas 13 – CRISPER associated protein 13 CMP Test – Comprehensive Metabolic Panel CNS – Central Nervous System
CPK-MB - Creatine phosphokinase myocardial band
CRISPR – Clusters of regularly interspaced short palindromic repeat CT – Computed Tomography
E-Protein – Envelop Protein ER – Endoplasmic Reticulum
G-CSF – Granulocyte Colony Stimulating Factor IFN – Interferon IgG – Immunoglobulin G IgM – Immunoglobulin M IL – Interleukin
IL-10 – Interleukin-10 IL-2 – Inteleukin-2
IL-6 – Interleukin-6
JAK-1 – Janus Kinase-1
JAK-STAT – Janus Kinase-Signal Translator and Activator of TranscriptionMCP-1 – Monocyte Chemoattractant Protein-1
MERS – Middle East Respiratory Syndrome NCDC – Nigeria Center for Disease Control
NF-Kb – Nuclear Factor kappa-Light-Chain-Enhancer of activated B cells. N-Protein – Nucleocapsid Protein
RDRP – RNA – dependent RNA polymerase RNA – Ribonucleic Acid
S1-Protein – Spike Protein domain 1 S2-protein – Spike Protein domain 2
SARS – Severe Acute Respiratory Syndrome S-Protein – Spike Protein
STAT-1 – Signal Transducer and Activator of Transcription-1
STAT-2 - Signal Transducer and Activator of Transcription-2
Th1 – Type 1 T helper cell
TNF-α – Tumor Necrosis Factor Alpha
DNA –Deoxyribonucleic Acid
ARDS- Acute Respiratory Distress Syndrome
CNS- Central Nervous System
CDC- Center for Disease Control
RIG-1- Retinoic Acid Inducible Gene-1
PAMPS- Pathogen Associated Molecular Patterns
MDA-5- Melanome Differentiation- associated Protein 5
ISGS- Interferon stimulated Genes

Introduction

Covid-19 also known as Corona Virus disease 2019 ("CO" for Corona, "V" for Virus, "D" for disease and "2019", the year it was identified) is an infectious respiratory illness caused by a newly discovered coronavirus called severe acute respiratory syndrome

coronavirus 2 (SARS-Cov-2) which is in charge of the current outbreak of pneumonia. This killer disease called coronavirus was first identified in 1965 by Tyrrell and Bynoe and belongs to the family 'coronaviridae" and subfamily "Orthocoronavirina" as the name suggests, whose members show characteristics of "crown-like" spikes on their surfaces with a diameter of 80-120nm [1]. The four types of this virus have been reported which include; Alphacoronavirus, Betacoronavirus, Delta coronavirus and Gamma coronavirus [2]. Seven strains of coronavirus have been identified as disease causing in humans. Among them, SARs- CoV and MERs-CoV have caused outbreak in the past and are regarded as highly pathogenic coronavirus that infect the lower respiratory tract for instance the lung tissue while other coronavirus (like 229E, Nl63, OC43, and HKUI) are associated with common cold and affect the upper respiratory tract like the nose and throat. SARS- CoV-2 is regarded as the seventh strain of Coronavirus family to induce infection in humans [3].The virus (SARs-Cov-2) belongs to the genus "betacoronavirus" group like MERs and SARs-Cov coronavirus. SARs-Cov and SARs-CoV-2 have approximately 79% genome sequence homology [4]. Studies have revealed that SARs-CoV-2 binds with angiotensin-converting enzyme-2 (ACE-2) which is similar to SARs-CoV, this is due to the similarity of the receptor-binding domain found on the spike protein. It uses the spike(s) protein found on their surface to recognize and bind to specific receptors on host cell surfaces resulting in virus entry to the cell host and causing disease [2]. Covid-19 is a typical crown-like appearance under an electron microscope due to the presence of glycoprotein spikes on its envelope and a zoonotic disease which was first identified on December, 2019 and was named by World Health Organization [5]. On 11th February, 2020. When Covid-19 first appeared in Wuhan City in Hubei province of China, it was an epidemic as it only spread locally in the country. Later, it spreads to many other countries and became a pandemic. This was declared by WHO on 11th March, 2020 [6]. Although it originated in China, cases have been confirmed all around world in the majority of European countries and from its epicenter moved from China to .Western Europe [7]. It continues to spread from one person to another via respiratory droplets produced during coughing and sneezing.

A wave in a pandemic implies a rising number of sick individuals, a defining arise and fall in trend. The outbreak shows different waves in different countries due to the preventive measures taken by the country, economy of the country and also the advancement and development of the country. Mutations and emergence of virus variant are some factors that contribute to multiple waves. The first wave is the beginning of the outbreak due to limited knowledge of the disease and inadequate specialized equipment. It represents a lots of cases and high peak of transmission but with preventive measures such as social distancing and quarantine, the number of cases tend to reduce, leading the population to a state of relaxation. This causes the resumption of economic and social activities leading to the second wave. The second wave is related to a slight rise in cases, due to failure to obtain general immunity followed by pharmacologic interventions such as vaccines [8].The third wave is the most recent wave, which is when there is a surge in the number of cases over a period of time in a particular region and has been documented in some countries. Covid-19 has been the major concern of physicians, public health specialists and researchers. Global public health initiatives are been implemented and rapid investigations of the biology of the virus and pathogenesis of covid-19 are being conducted on research institution all round the world [9].

Origin and Transmission of COVID -19: Covid-19 originated from the Hunan seafood market at Wuhan, South China where raccon dogs, bats, snakes, and some other animals are sold and rapidly spread up to109countries. Though the zoonotic source of SARS – COV-2 has not been confirmed, the sequence based analysis suggests that bat is the main reservoir; the recombination of DNA was found to be involved at spike glycoprotein which assorted SARS-COV-2 with the receptor binding domain (RBD) of another Beta coronavirus. This could be the reason for cross-species transmission and rapid infection [10]. SARS-COV-2, the virus that causes covid-19 is a highly transmittable and pathogenic viral infection and is mainly transmitted through contact with respiratory droplets [11,10]. Primarily, covid-19 can spread through contact with infected ones. A single cough from an infected person can circulate up to 3,000 droplets. These droplets can land on other people and covering surfaces around them. Covid-19 can be spread by close contacts with small droplets released from infected individual's upper respiratory tract secretion e.g sneezing and coughing. It can also be transmitted through surface contamination, when these droplets land in objects and surfaces around the person and other individual touches these objects or surfaces and further touching their eyes, nose or mouth [9]. Recently a study reported that the virus can remain viable in aerosols and plastic for 3 hours and 72hours before decrease in infection respectively. There is a possibility of becoming infected via the fecal-oral route; this is supported by detection of the virus in stool sample even after nasopharyngel swab. Also asymptomatic individuals can act as infection vectors that are why self -Isolation and social distance practice is recommended.

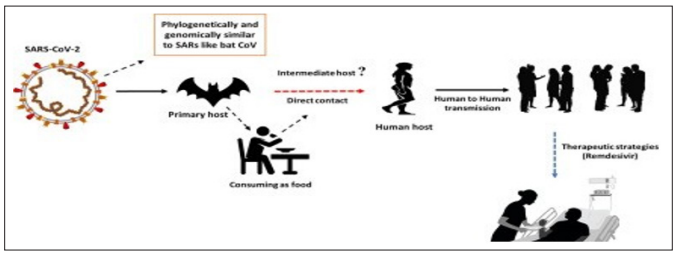

Figure 1: Origin and transmission of Covid-19

Epidemiology

According to the data generated by the World Health Organization (WHO) Coronavirus disease (COVID-19) dashboard, one hundred and thirty million, four hundred and fifty nine thousand, one hundred and eight four (130, 459, 184)confirmed Covid-19 cases had been reported, including two million ,eight hundred and forty two thousand, three hundred and twenty five (2,842,325) deaths. Of note, 11 percent cases are fatal. Incidents have occurred in more than 215 countries to date. There are fifty six million, five hundred and eighty nine thousand, one hundred and ninety (56, 589, 190) confirmed cases in the Americas, 45, 877, 941 in Europe, 15, 212, 235 in south-East Asia, 7,693,094 in Africa, and 1,965,683 in the Western pacific. The highest fatal cases have been recorded in the Americas, followed by Europe and South-East Asia [12].

Figure: 1 Number of Confirmed Cases Covid-19 By Who Globally

CONTINENT	CONFIRMED CASES
Americas	56,589,190
Europe	45,877,941
South-East Asia	15,212,235
Africa	7,693,094
Western Pacific	1,965,683

Mechanism of entry and replication of sars-cov-2 inside the human cell

The virus enters the body through the nose, eyes or mouth. The spike protein binds specifically to the Angiotensin-converting enzyme 2(ACE-2) receptors present on the type 2 pneumocytes in the alveoli of the lungs, just like SAR-COV-1 but SARS-COV-2 have a higher affinity for it which help a faster human to human spread [12]. The type 2 pneumocytes produce surfactants (a Lipo protein in the tissue of the lung that reduces surface tension and permit more efficient gas transport) which will reduce the collapsing pressure and also decrease the surface tension in the alveoli [13,14]. Expression of the ACE2 receptors is found in many extra pulmonary tissues including the heart, kidney, endothelium and the intestines, but the lungs is the most vulnerable ACE-2-expressing tissue due to the fact that they represents a large surface area which an inhaled virus can infect and the ACE2 –expressing lung cells have higher level for viral process-related genes, which facilitate corona viral replication. It also functions as a co-receptor for nutrients intake in the luminal surface of intestinal epithelial cells. The binding of the ACE-2 receptor allows the entry of the virus into the host cell due to host cell proteases that cleave the spike protein of the virus .The virus will enter the host cell by direct cell entry membrane fusion or by endocytosis [15].

SARS COV-2 releases its positive-sense RNA into the host cell cytoplasm. The RNA will be translated into polyproteins, ppla and pplb (two long polypeptides) which help in the replication and transcription of the viral RNA. The replication of positive-sense RNA using RNA-dependent RNA polymeras enzymes gives a negative-sense RNA. The negative sense RNA is either replicated to give positive-sense RNA (Incorporated in the viral genome) or transcribed. The transcribed messenger RNA can be translated to produce viral proteins like the spike, membrane envelope and nucleocapsid proteins [16]. The proteins will be carried by the host cell endoplasmic reticulum to the golgi apparatus, where they will be packaged into vesicles and assembled near the host cell membrane. The new viruses that are formed exit the host cell by exocytosis to infect other cells. This process results in death of the host cell.

Summary in the Replication of SARS-COV-2 Inside the host cell:

Attachment to host cell ACE-2 receptor. Entry in the host cell by membrane fusion. Uncoating of the virus and release of genomic positive sense RNA in host cell cytoplasm and replication of RNA to give negative RNA. Replication of negative –sense RNA gives back the positive sense RNA which is incorporated in the new virus. Transcription of negative RNA to give viral protein. Packaging in golgi bodies and assembly of viral protein and the viral genomic RNA. Exocytosis.

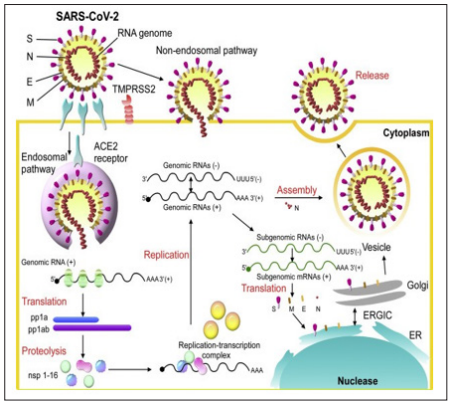

Figure 2: Mechanism of entry and replication of SARS-Cov-2 inside the human cell

Pathogenesis of COVID-19

The symptoms of Covid -19 can be divided into three stage:-

The first stage becomes the asymptomatic (no signs) and lasts for 1 to 2 days after being infected and this is the attachment of virus to the ACE-2 receptors and replicates. The virus can be detected by the swab test, nasal swabs being more effective than throat swabs. There is a limited innate immunity response in the stage.

The second stage is the infection of the upper respiratory airways and migrates down the respiratory tract. An innate immune response is triggered [17].

The third stage is the final, the acute respiratory distress syndrome (ARDS) and Hypoxia, in which the virus reaches, infects and damages the alveoli in the lungs which release interferon that signal the nearby healthy cells to release antiviral peptides [.18.] The antiviral peptides cause the breakdown of the virus. The damaged cells release danger molecules (called damaged – associated molecular pattern, protein-associated molecular patterns and cytokines) that activate the innate immune system for phagocytosis [19]. The macrophages receive the signal from the damaged cell and release fluids and fill the capillary and alveolus (the area responsible for gas exchange). The neutrophils also target the site of infection and thereby killing of viruses and damage the healthy pneumocytes. This leads to a decrease in the surfactant present in the alveolus. These phagocytic cells also release inflammatory mediators, like 1L-2,1L-6,1L-10, TNF-α, G-CSF, and Mcp-1 all of which causes inflammation[20,21]. This hyperactive immune response of the body is called a cytokine storm. This affects the gas exchange of the alveoli and lead to hypoxemia and ARDS. For severe infection, the protein-rich fluid may enter the bloodstream, and cause systemic inflammatory response syndrome (SIRS), which can further lead to multi-organ failure [22].The cytokines will also lead to increased level of procoagulants, leading to pulmonary embolism [23]. Also, the infection activates receptors on the cranial nerve and the CNS generates a cough response. Finally, the inflammatory mediators can also act in the hypothalamus in the brain leading to fever.

Symptoms

According to World Health Organization (WHO), on average, after being infected, it takes 5-6 days for symptoms to become visible [24]. The major organs affected are lungs, heart, liver, kidney, intestines and the brain and the most severe effect of Covid-19 is ARDS due to improper blood circulation and the weakening of blood vessels all over the body. Also, widespread distribution of ACE-2 receptors can lead to organ injury and cause multi-system organ failure. Hence, people with unhealthy blood vessels such as smokers and people with conditions like high blood pressure, cholesterol, diabetes and cardiovascular diseases are more at risk of Covid-19 [25].

Common symptoms of covid-19 are fever or chills, dry cough, weakness, headache, congestion or runny nose, nausea or vomiting.

The less common ones are body ache, sore throat, diarrhea, conjunctivitis; skin rashes .The very severe symptoms are shortness of breath, chest pain, and loss of speech, inability to stay awake, bluish lips or face.

The following conditions make up the high risk category of Covid-19 according to Centers for Disease Control and prevention (CDC):-immuno-compromization, Liver disease, chronic lung disease, chronic kidney disease that has been treated with dialysis, asthma ,diabetes, people aged 65 years and older etc.

Immune Response Against COVID-19

The little understanding and knowledge concerning specific immune responses against SARS-COV-2 threw much challenges to the development of vaccines. The virus has an asymptomatic phase of incubation period of 2 to 14 days after infection. It has higher inclination towards ACE-2 receptor in the lungs. The report has emphasized the complex rule of antibody dependent enhancement (ADE) in the pathogenesis of the virus and has played major concern in development of vaccines and antibody therapeutics. Currently, there is no conclusive evidence that suggests the occurrence of ADE in 2019-ncov infection. Hypothetic views are drawn depending upon previous reports of SARS and MERS coronavirus.

Usually, innate immune cells recognize viral invasion by detecting pathogen- associated molecular patterns (PAMPS). In the cases of RNA viruses like coronavirus, PAMPS are detected by RIG-1 (Retinoic acid-inducible gene-1) or MDA-S (Melanome differentiation-associated protein-5).

This detection will triggers the production of NF-kB (nuclear factor-Kb) via signaling cascade followed by translocation of activated NF-Kb into the nucleus. On the other hand, E3 Ubiquitin kinases phosphorylate, both IRF3 (interferon regulatory factor-3) and IRF7 (interferon regulatory factor-7) on entry to nucleus initiate the expression of type 1 interferons (IFNS), which will bind to the IFNAR (IFNα and B-receptor) and activate the JAK-STAT signaling pathway and result in phosphorylation of STAT 1 and STAT 2 due to JAK 1 and tyrosine kinase-2 (TYK2) kinases. Later, the phosphorylated STAT1 AND STAT2 bind with interferon regulatory factor-9 (IRF-9).This complex enters the nucleus and starts the expression of ISGS (interferon stimulated genes). This expression of pro-inflammatory cytokines, interferons, and IFN-stimulated genes collectively act as an innate antiviral immune response, which helps in limiting viral replication in infection for Adaptive response, during viral infection, Th1-type immune response is mainly responsible for adaptive immunity. Generation of the cytokine due to antigen presenting cells usually regulates the direction of T-cell response. Adaptive immune is coordinated by T helper cells while cytotoxic T cell kills those cells that are infected by the virus. Humoral immunity, also known as antibody-mediated immunity significantly limits the rate of infection and further prevents re-infection from the same virus. Reports reveal the presence of 1gG and Nabs (neutralizing antibodies) even after two years of infection) [26]. Immunoglobulin M was observed at ninth day of infection followed by IgG by week two [27].

The waves of covid-19 pandemic

The first wave following the surge of the virus in 2019 heavily affected almost every corner of planet although countries affected may differ by the spread due to differences in seasons as Southern hemisphere was affected later. Due to minimal infection, that time mainly young people were infected, some people thought that it was over and relaxed in the implementation of the preventive measures and led to escalated number of confirmed cases. That led to the second wave of the pandemic. The second wave according to experts had a higher force as a result of appearance of new variants and increased number of cases in intensive care units. The third wave from Dr N K Arora expressed the change in virus in form of mutations and deceptive antibodies when vaccination is done slowly [25]. This is the era of highly contagious Delta variant which the scientists have named B.1.617 and is detected in 92 countries. The wave affected different cities at different time intervals. The third wave is influenced by trends in the nearly half of the world confirmed covid-19 cases, despite only comprising 14 percent of the global population [28]. The effect of this virus on the social determinants of health is one of the major global health crisis [29]. The third wave is the third peak of this pandemic and it is regarded as the third increased of confirmed cases of the pandemic. There are million people across South Asia, the Middle East, South America and African continents that have been confirmed with increased number cases due to third wave of covid-19. It takes only 2 to 3 days for the virus to damage the lung compared to the first and second wave that it takes 10 days and 5 to 7 days respectively. This is due to mutations made by the variants of this virus. The most likely drivers of third wave are behavior change especially during holiday travel and large events such as social gathering, reduced adherence to non- pharmaceutical interventions like mask wearing, ongoing viral mutation, seasonal factors like cold weather over the winter months, could increase transmission due to increased contacts indoors, and decreased ventilation, re-infection due to the waning of immunity conveyed by previous infection. But adherence to the precautionary measures can help to reduce the increase number of cases leading to decrease in number of cases during the third wave and also prevent the emergence of fourth waves as predicted by experts.

Effects of Third Wave and Covid-19 Pandemic in Our Daily Life

Covid-19 has affected our day to day activities and is gradually slowing down the global economy. It has affected thousands of people who are either sick or are being killed due to the spread of the disease. People are living in fear and anxiety, businesses have been affected, and World trade and movements have been disrupted. Various industries like pharmaceutical industries, solar power sector, tourism, information and electronics industry have also been affected by Covid-19 pandemic .Currently, the impacts of Covid-19 in our daily life are extensive and have far reaching consequences. These can be divided into various categories;- Health Care: Challenges in the diagnosis, quarantine and treatment of suspected or confirmed case.

Age Distribution and Diversity of Third Wave of Covid-19 Pandemic

According to World Health Organization, Pediatric cases have been reported but their symptoms are mild .Most of the infected individuals are 30 years old and older suggesting that the elderly person are especially at risk of developing more severe symptoms and even more at risk of death [30]. Experts said that children are at lower risk of being infected by the virus because they have less of ACE2 receptors in their lungs. Less morbidity like absence of cardiac- disease, hypertension, obesity etc. but children with the above mentioned complications have a high risk of being infected. The symptoms may be asymptomatic or mild and can be transferred from one person to another. Infection during pregnancy has also been reported but initial reports suggests that intrauterine transmission of virus is not likely even if the infection happen late in the pregnancy as it was not found in the amniotic fluid, cord, blood, neonatal swab and breast milk [31,30].

Treatment and Supportive Therapy

Treatment is basically supportive and asymptomatic. The first step is to guarantee sufficient isolation to stop spread to other not contacted individuals, cases and health care workers. Suspected cases should be isolated in a single room or self-isolated at home subsequent to the doctor's advice. Confirmed patients can be cohorted in the same ward. Critical patients should be admitted to ICU immediately. Common strategies involve bed rest and palliative therapy, supplying enough calorie and water consumption, sustaining water-electrolyte balance and

homeostatic, scrutinizing vital signs and oxygen saturation.

Symptomatic therapy: The mild disease should be managed at home by advising about dangerous signs. The standard approach is continuing hydration, nutrition and managing fever and cough. If a patient has a high temperature exceeding 38.5oC with noticeable distress bodily cooling or antipyretic medicine therapy would be given.

Antiviral therapy: There has not been currently, yet widely accepted therapeutic option for Covid-19 disease. Antiviral drugs such as ribavirin, Lopinavir-ritonavir, have been tried depending on the anecdotal knowledge with HIV, SARS and MERS infection therapies. Other suggested drugs for Immunotherapy are Intravenous Immunoglobulin (IVIG), interferon, and convalescent immune plasma of improved cases from Covid-19 disease.

Precautionary Measures: Third Wave Pandemic of Covid-19 can entirely be prevented by taking the following precautionary measures:

Physical Distancing: Social distancing as well as maintaining at least 6 feet from one another can prevent the spread of Covid-19 as it can only spread through close contact with the respiratory droplets of an infected person like cough.

Face Masks: Face mask aids in containing respiratory droplets that transmit SARs- Cov-2 from asymptomatic carrier. Research has proved that mask can be fairly effective in thwarting contagious from getting into the nose and mouth.

Hand Hygiene: Hand washing is one of the most efficient ways to prevent germs from spreading. Clean hands can stop gems from spreading from one person to another. It is recommended by medical professionals to follow the following steps for proper washing of hands. Firstly, dampen your hands with clean running water then turn off the tap and apply soap. Lather your hands by rubbing them together with the soap and make sure to scrub clean back of your hands, between your fingers and under your nails. Scrub your hands for at least 20 seconds. Rinse your hands well under clean, running water. Dry your hands well under clean towel or air dry them. Though there is no substitute to washing hands with soap and water, but in situation where it is feasible, alcohol based hand sanitizer with at least 60% alcohol can be used.

Lock Down: Depending on the economic situation of a country, complete or smart lockdown can be imposed to break the transmission of Covid-19. Lockdowns disrupt the transmission cycle of disease by confirming maximum number of infected personnel to an identified disease hotspot with an aim to retarding spread of Covid-19 in that specific locality. Those infected should be isolated to avoid the spread of the disease. Vaccination: Vaccines are considered as the best method to remain safe against Covid-19 pandemic. They are being introduced rapidly in the world's market today against Covid-19.

Laboratory Diagnosis of COVID-19: The major categories of diagnostic methods available today for Covid-19 include: Molecular testing: Direct detection of the virus can be achieved by identifying antigen or the viral genome. Reverse transcription polymerase chain reaction (RT-PCR) assay is the most common and reliable test with relatively high specificity. The test involves purifying the viral genome from the throat swab and amplifying it using primers specific to the SARS- COV-2 Virus, usually the RDPR, N and E genes are used for the identification of the virus. The only disadvantage to this method is that it takes time [32]. Serological investigation: This can also be performed by taking the blood, plasma or serum of the patient and testing it for 1Gg antibodies (the proteins made due to the immune response of the body to the viral antigens). The IgM antibodies become detectable around the 7th day of infection and present in the blood until the 3rd week of infection. On the other hand, IgG appear during the 2nd week of infection and remain in the blood to provide long term immunity [33]. One of the disadvantages of using this technique is that diagnosis can only be done when the patient is in the recovery phase and the patient might have transmitted the virus to other during that time. It also gives false positive result after the patient recovers by detecting long-term antibodies in the blood [34, 35].

Radiological Imaging: Chest X-rays and CT Scans are supplementary tests used with RT-PCR test to see the progression and damage done by the virus, though CT Scans and X- rays do not always indicate. CT scans have been reported to show similar patterns of ground glass opacity indicating damaged lungs, inflammation, and pneumonia [36]. In fact, not all patients develop symptoms like pneumonia that CT scan would fail in diagnosis.

Higher Enzymatic Marker: Unlocking (Sherlock): is a rapid test which is used for the diagnosis. A sample is taken from the upper airway of suspected Covid-19 patients. The RNAs in sample are amplified and reporter genes are added. CRISPR-Cas 13 is then added along with a guide RNA (which is designed to target the viral RNA). Cas 13 activates its cleaving mechanism when the viral is found and starts cleaving nearby RNAs and reporter genes randomly. Each end of the receptor carries a different fluorescent label and so their cleavage generates a signal if the virus RNA is present. The sample is then applied on lateral flow assay device. Two bands are obtained if the receptor gene is not cleaved (when viral RNA is absent) [37,38].

LumiraDX antigen machine: This is diagnostic point of care machine that performs a test and provides results within minutes rather than hours and reduce the testing load on central hospitals. They are antibody and antigen principle which runs on a wall outlet or battery-powered multi-assay point of care instrument. Nasal and nasopharyngeal swab samples are extracted using the extraction buffer and a transfer via dropper that delivers 20 micro liter onto a test strip. It takes 12 minutes to deliver a positive or negative test result. The instrument plat for has a touch-screen interface and connects to a cloud server for uploading test data into electronic medical records.

Haematological makers like complete blood count (CBC) test; it would show thrombocytopenia, and lymphopenia, high white blood count (WBC) and high neutrophil count. Biochemical makers like; CMP test: kidney damage would result in high urea creatainine level. Cardiac Troponin 1 and CPK-MB test: Elevated levels of these indicate myocardial damage. LFT: Increased levels of Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) enzymes.

Conclusion

Covid-19 is real and should not be ignored. Even as the pandemic is still ongoing, the disease is surrounded with numerous uncertainties. Although the progress made by scientists is undeniable, new properties of the virus are emerging and certain problems remain unanswered, for example, the possibility of recurrent infection, the possible persistency and the capability

of the virus to infect different cell types and cause complication outside the respiratory tract, and lack of specific vaccines and therapeutics for SARs-Cov-2.

Recommendations: We recommend that the public should adhere strictly to the preventive measures, Covid-19 vaccine should be made easily available and ensured that everyone is vaccinated. Also, further investigation should be done on the cause, and effects of different waves of Covid-19 pandemic.

Acknowledgment: We wish to thank the followings persons; Ali Faith C, Okolo Raphael. C, Ugwu Ifeanyichukwu. B and Okoro Beatrice.N for their tireless efforts towards the publication of this review. Also we want to appreciate the citations adopted in this paper.

References

1. Perlman S. Another Decade (2020) another coronavirus. New England Journal of Medicine 382: 760-762.
2. Wang, Y., Wang, Y., Chen, Y. and Qin, Q (2020) Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (Covid-19) implicate special control measures. Journal of Medical Virology 92: 568-578.
3. Zhu N, Zhang D, Wang W, Li X, Yang B (2019) A novel coronavirus from patients with pneumonia in China. New England of Journal of Medicine 382: 727-733.
4. Chen N, Zhou M, Doug X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395: 507-513. World Health Organization (2020) Landscape analysis of therapeutics on 21st March, 2020.
5. Ahmed W, Angel N, Edson J, Bibbby K, Bivins A (2020) First confirmed detection of SARS-COV-2 in untreated waste water in Australia: A proof of concept for the waste water surveillance of COVID-19 in the community. Science of the Total Environment 728: 138764.
6. Sokolovska L, Sultanova A, Cistjakovs, M Munuska M.J (2020) Covid-19: the third wave of coronavirus infection outbreak J. Transl. Sci 7: 1-5.
7. Pfaar O, Klimek L, Jutel M, Akdis CA, Bousquet J, et al. (2021) Covid-19 Pandemic: Practical considerations on the organization of an allergy clinic – An EAACI/ARIA Position Paper. Allergy 76: 648-676.
8. Hafeez A, Ahmed, S Siddaui, S.A, Ahmad M, Mishra, S (2020) A review of Covid-19(Coronavirus disease 2019) diagnosis, treatment and prevention EJMO 4: 116-125.
9. Shereen, M.A, Khan, S., Kazmi, A, Bashir N, Siddique R (2020) Covid-19 Infection: Origin, transmission and characteristics of human coronaviruses Journal of Advanced Research 24: 91-98.
10. Joseph, A.A. and Joseph, A.O (2020) Beliefs and Perceptions about Covid-19 among students of a higher institution in South-Western Nigeria. Journal of Medical and Biomedical Science 1: 72-80.
11. Zeyaullah M D, Abdullah M Alsharni K, Ahmad, I, Alams Khan, W.H, Ahmad (2021) R. Covid-19 and SARs-Cov-2 Variants: Current Challenges and Health Concerns. Frontiers in Genetics 3: 667-670.
12. Bombardini, T. and Picano, E (2020) Angiotensin converting enzyme 2 as the molecular bridge between epidemiologic and clinical features of Covid-19. Canadian journal of Cardiology 36: 784-el. Mirastchijski, V, Dembiriski R, Maedler K (2020) Lung surfactant for pulmonary barrier restoration in patients with Covid-19 pneumonia. Frontiers in Medicine 7: 254.
13. Wang H, Yang P, Liu K, Guo F, Zhang, Y, et al. (2008) SARs Coronavirus entry into host cells through novel clathrin and caveolae-independent endocytic pathway-Cell Research 18: 290-301.
14. Nakagawa K, Lokugamage, K.G, Makino S(2016) Viral and Cellular Mrna translation in Coronavirus infected cells. Advances in Virus Research 96: 165-192.
15. De Masson A, Bovaziz J. D, Sulimovic L, Cassius C, Jachiet, M, et al. (2020) Chilblains is a common cutaneous finding during the Covid-19 pandemic: A reterospective nationwide study from France. Journal of the American Academy of Dermatology 83: 667-670.
16. Badraoui R, Alrashedi MM, El-May MV, Bardalici F (2020) Acute respiratory distress syndrome: a life threatening associated complication of SARS-Cov-2 infection inducing Covid-19. Journal of Biomolecular Structure and Dynamics10: 667-670. Mogensen, T.H (2009) Pathogen recognition and inflammatory signaling in innate immune defenses. Clinical Microbiology Reviews 22: 240-273.
17. Costela-Ruiz VJ, Illescas-Montes, R, Puerta-Puerta J.M, Ruiz C, Melguizo Rodriguez L(2020) SARS-Cov-2 Infection: The role of cytokines in Covid-19 disease, cytokine and growth factor review 54: 62-75.
18. Golchin, A, Seyedjafari, E, Ardeshirylajimi, A (2020) Mesenchymal stem cell therapy for Covid-19: Present or future. Stem Cell Reviews and Reports 16: 427- 433.
19. Polidoro, R.B, Hagan R.S (2020) Desantis Santiago, R. and Schmidt, N.W. Overview: Systematic inflammatory response derived from lung injury caused by SARs-Cov-2 infections explains severe outcomes in Covid-19. Frontiers in Immunology 11: 1626.
20. Jose R J, Manuel A (2020) Covid-19 Cytokine Storm. The interplay between inflammation and coagulation. The Lancet Respiratory Medicine 8: e46-e47.
21. Zothantluanga J.H, Latthanzara H, Shakya A, Lalmawizuala, JH (2020) Covid- 19 incidence in Mizoran, India-Sci vis 20: 93-105.
22. Kumar M, Patel AK, Shah A.V, Raval J, Rajpara, N, Joshi, M et al. (2020) First proof of the capability of Waste Water Survellence for Covid-19 in India through detection of genetic material of SARs-Cov-2. Science of the Total Environment 746: 141326.
23. Liu J.P, LI AC, XU KH, Velozzi D.M, Yang S, et al. (2006) Sedimentary features of the Yanghe River-derived along shelf Clinoform deposit in the East China sea-continental shelf Research 20: 2141-2156.
24. Rauf A, Abu-Izneid T, Olatunde A, Ahmed Khalil A, Alhumaydhi, F.A., et al. (2020) Covid-19 Pandemic: Epidemiology, etiology, conventional and non-conventional therapies – International Journal of Environmental Research and Public Health 17: 8155.
25. Haddad, M, Johnen, C, Kohler S (2020) Polynomial silent Self-stabilizing P-star decomposition. The Computer Journal 63: 253-266.
26. Fisayo T, Tsukagoshi, S (2021) Three Waves of Covid-19 Pandemic Post Graduate Medical Journal 97: 332-332.
27. Wang W, Tang J, Wei, F (2020) Updated understanding of the outbreak of 2019 novel coronavirus (2019-ncov) Medical virology 92: 441-447.
28. Lu,, Shi Y (2020) Coronavirus disease (Covid-19) and neonate. What neonatologist need to know. Journal of Medical Virology 2: 564-567.
29. Udugama, B, Kadhiresan, P, Kozlowski H.N, Plalekjahani, A,

Osborne, M, et al. (2020). Diagnosing Covid-19: the disease and tools for detection. ACS nano 14: 3822-3835.

30. Jacofsky, D, Jacofsky EM, Jacosfsky M (2020) Understanding antibody testing for Covid-19. The Journal of arthroplasty 35: 574-581.
31. Pavlova, I.P, Nair,S.S, Kypiranuo, Tewari AK (2020) The rapid Coronavirus antibody test: can we improve accuracy? Frontiers in Medicine 2020: 7.
32. Ragnesola, B, Jin D, Lamb C.C, Shaz, B.H, Hillye, C. D et al. (2020) Covid-19 antibody detection using lateral flow assay test in a cohort of convalescent plasma donors. BMC research note 13: 1-7.
33. Meng, H, Xiong, R, He, Rylin W, Hao, B, Zhang, L, Lu, Z, et al. (2020) CT Imaging and Clinical Course of asymptomatic cases with Covid-19 pneumonia at admission in Wuhan, China. Journal of Infection 81: e33-e39.
33. Kumar, V, Doshi, K.U, Khan, W.H, Rathore A.S (2021) Covid-19 Pandemic: Mechanism, diagnosis, and treatment. Journal of Chemical Technology & Biotechnology 96: 299-308.
34. Xiang X, Qian, ky Zhang Z, Lin, F, Xie, Y, Liv Y, et al. (2020) CRISPR-Cas systems based molecular diagnostic tool for infectious diseases and emerging 2019 novel coronavirus (Covid-19) pneumonia. Journal of drug targeting 28: 727-731.